REMARKS

At the outset, applicant would like to thank Examiner Davis for her time and consideration of the present application at the interview with the undersigned attorney. At the interview, the issues raised in the outstanding Official Action were discussed.

In the outstanding Official Action, claims 15-17 and 19-20 were rejected under 35 USC §102(b) as allegedly being anticipated by NAUGHTON et al. 4,963,489. Claims 15-17 and 19-20 were rejected under 35 USC §102(e) as allegedly being anticipated by LEE et al. 6,139,578. Claims 15-20 were rejected under 35 USC §103(a) as allegedly being unpatentable over NAUGHTON et al. or LEE et al. These rejections are respectfully traversed.

NAUGHTON et al. disclose a three-dimensional cell culture system wherein the stromal support matrix predominantly comprises fibroblasts. The addition of macrophages is optional. This three-dimensional cell system may be used as an implantable system once the appropriate cells have been grown to maturity (column 3, lines 26-36).

The LEE et al. publication is directed to a synthetic, poorly-crystalline apatitic (PCA) calcium phosphate material seeded with cells. This material is porous and may be seeded with macrophages (see column 10, lines 26-34). However, it is disclosed that the seeding of this material with macrophages is intended for purposes of *in vitro* studies. There is no mention

in the document that the PCA calcium phosphate material seeded with macrophages could be used for preparing humanized biomaterial.

Applicant believes that both publications fail to disclose or suggest the claimed humanized biomaterial. At this time, the Examiner's attention is respectfully directed to claim 15 which is directed to a humanized biomaterial comprising a porous biocompatible composite material customized and implanted with monocyte derived cells. The monocyte derived cells are substantially irreversibly bound to the biomaterial. The monocyte derived cells are macrophages, wherein said macrophages are human patient's macrophages obtained by *ex vivo* differentiation from blood monocytes leading to living macrophages, and are cultured under conditions enabling their penetration and adherence into biomaterial, with the porous biomaterial, allowing infiltration of the biomaterial with a substantially irreversible binding of the living macrophages to the biomaterial, being humanized with patient's macrophages and ready for implantation.

As a result, the claimed macrophages have not developed tissue specificities and present different phenotypic and functional characteristics from tissue resident macrophages present in low numbers of colonizing cells.

The fixation of *ex vivo* differentiated, non-proliferating macrophages to a biomaterial therefore induces

effects favoring the proliferation of tissue cells. This is distinct from NAUGHTON et al. or LEE et al. who are colonizing biomaterials with proliferating cells eventually contaminated with macrophages corresponding to the targeted tissue.

As invited by the Examiner at the interview, applicant submits as an attachment with this amendment a declaration that demonstrates that the claimed humanized biomaterial is distinct from the teachings of NAUGHTON et al. or LEE et al.

As a result, applicant believes that NAUGHTON et al. or LEE et al. both fail to anticipate or render obvious the claimed invention.

In view of the present amendment and the foregoing remarks, therefore, applicant believes that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on this basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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PD/lrs

APPENDIX:

The Appendix includes the following items:

- declaration signed by Dr. Jacques BARTHOLEYNS
- Gordon, S., "Alternative Activation of Macrophages", Native Reviews-Immunology, Vol. 3, January 2003
- Willenbring, H. et al., "Myelomonocytic cells are sufficient for therapeutic cell fusion in liver", Nature Medicine, Vol. 10, No. 7, July 2004
- Bomstein, Y. et al., "Features of skin-coincubated macrophages that promote recovery from spinal cord injury", Journal of Neuroimmunology, 142, (2003), pp. 10-16